Complete Summary

GUIDELINE TITLE

Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease.

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization, National Heart, Lung and Blood Institute; 2006. 88 p. [560 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung and Blood Institute (NHLBI). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization, National Heart, Lung and Blood Institute; 2005. 115 p.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 12, 2007, Ketek (Telithromycin) (Update): Two of the three previously approved indications, acute bacterial sinusitis and acute bacterial exacerbations of chronic bronchitis, were removed from the prescribing information because the balance of benefits and risks no longer support approval of the drug for these indications. In addition, warnings were strengthened for hepatotoxicity (liver injury), loss of consciousness, and visual disturbances.
- December 8, 2006, Heparin Sodium Injection: Revisions to the WARNINGS section of the prescribing information for Heparin to inform clinicians of the possibility of delayed onset of heparin-induced thrombocytopenia (HIT), a serious antibody-mediated reaction resulting from irreversible aggregation of platelets.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic obstructive pulmonary disease (COPD)

Note: It is not the scope of this report to provide a comprehensive discussion of the natural history of comorbidities associated with COPD but to focus primarily on chronic airflow limitation caused by inhaled particles and gases, the most common of which worldwide is cigarette smoke. However, chronic airflow limitation may develop also in nonsmokers who present with similar symptoms and may be associated with other diseases, e.g., asthma, congestive heart failure, lung carcinoma, bronchiectasis, pulmonary tuberculosis, bronchiolitis obliterans, and interstitial lung diseases. Poorly reversible airflow limitation associated with these conditions is not addressed except insofar as these conditions overlap with COPD.

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants

Physicians
Public Health Departments
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

- To increase awareness of chronic obstructive pulmonary disease (COPD) and decrease morbidity and mortality from the disease
- To improve prevention and management of COPD through a concerted worldwide effort of people involved in all facets of health care and health care policy
- To encourage an expanded level of research interest in this highly prevalent disease
- To work toward combating the nihilistic attitude toward COPD by disseminating information about available treatments (both pharmacologic and nonpharmacologic) and by working with a network of experts—the Global Initiative for Chronic Obstructive Lung Disease (GOLD) National Leaders—to implement effective COPD management programs developed in accordance with local health care practices

TARGET POPULATION

Individuals with chronic obstructive pulmonary disease

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis

1. Initial diagnosis:
    - Assessment of symptoms
    - Medical history
    - Physical examination
    - Measurement of airflow limitation using spirometry
    - Assessment of severity
    - Additional investigations, including bronchodilator reversibility testing, chest x-ray, arterial blood gas measurement, alpha-1 antitrypsin deficiency screening
    - Differential diagnosis
2. Ongoing monitoring and assessment:
    - Monitoring disease progression and development of complications
    - Monitoring pharmacotherapy and other medical treatment
    - Monitoring exacerbation history
    - Monitoring comorbidities

Risk Factor Reduction

1. Smoking prevention and cessation
2. Reduction of occupational exposures
3. Reduction of exposure to indoor/outdoor air pollution

Manage Stable Chronic Obstructive Pulmonary Disease (COPD)

1. Patient education
2. Pharmacologic treatment:
    - Bronchodilators (beta2-agonists, anticholinergics, methylxanthines, combination therapy)
    - Glucocorticosteroids (oral and inhaled)
    - Other pharmacologic treatments
3. Non-pharmacologic treatment:
    - Pulmonary rehabilitation
    - Oxygen therapy
    - Ventilatory support
    - Surgical treatments, including bullectomy, lung volume reduction surgery, lung transplantation

Management of Exacerbations

1. Diagnosis and assessment of severity:
    - Medical history
    - Assessment of severity
    - Differential diagnosis
2. Home management:
    - Bronchodilator therapy
    - Glucocorticosteroids
    - Antibiotics
3. Hospital management:
    - Assessment of symptoms, blood gases, and chest x-ray
    - Controlled oxygen therapy
    - Bronchodilators
    - Glucocorticosteroids
    - Antibiotics
    - Ventilatory support
    - Discharge and follow-up

MAJOR OUTCOMES CONSIDERED

- Mortality
- Morbidity, including physicians visits, emergency department visits, and hospitalizations
- Economic cost and social burden

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Preparation of Yearly Updates

Immediately following the release of the first Global Initiative for Chronic Obstructive Lung Disease (GOLD) report in 2001, the GOLD Executive Committee appointed a Science Committee, charged with keeping the GOLD documents up-to-date by reviewing published research, evaluating the impact of this research on the management recommendations in the GOLD documents, and posting yearly updates of these documents on the GOLD Website. The first update to the GOLD report was posted in July 2003, based on publications from January 2001 through December 2002. A second update appeared in July 2004, and a third in July 2005, each including the impact of publications from January through December of the previous year.

Producing the yearly updates began with a PubMed (http://www.nlm.nih.gov) search using search fields established by the Science Committee: 1) COPD OR chronic bronchitis OR emphysema, All Fields, All Adult, 19+ years, only items with abstracts, Clinical Trial, Human, sorted by Author; and 2) COPD OR chronic bronchitis OR emphysema AND systematic, All Fields, All Adult, 19+ years, only items with abstracts, Human, sorted by Author. In addition, publications in peer-reviewed journals not captured by PubMed could be submitted to individual members of the Science Committee, provided that an abstract and the full paper were submitted in (or translated into) English.

The publications that met the search criteria for each yearly update (between 100 and 200 articles per year) mainly affected Chapter 5, Management of COPD. Lists of the publications considered by the Science Committee each year, along with the yearly updated reports, are posted on the GOLD Website, www.goldcopd.org.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Description of Levels of Evidence

A. Randomized controlled trials (RCTs). Rich body of data.
   Definition: Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B. Randomized controlled trials. Limited body of data.
   Definition: Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.

C. Nonrandomized trials. Observational studies.
Definition: Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D. Panel consensus. Judgment.
Definition: This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Nominal Group Technique)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In January 2005, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Science Committee initiated its work on a comprehensively updated version of the GOLD report. During a two-day meeting, the committee established that the report structure should remain the same as in the 2001 document, but that each chapter would be carefully reviewed and modified in accordance with new published literature. The committee met in May and September 2005 to evaluate progress and to reach consensus on the messages to be provided in each chapter. Throughout its work, the committee made a commitment to develop a document that would reach a global audience, be based on the most current scientific literature, and be as concise as possible, while at the same time recognizing that one of the values of the GOLD report has been to provide background information on chronic obstructive pulmonary disease (COPD) management and the scientific principles on which management recommendations are based.

In January 2006, the Science Committee met with the Executive Committee for a two-day session during which another in-depth evaluation of each chapter was conducted. At this meeting, members reviewed the literature that appeared in 2005—using the same criteria developed for the update process. The list of 2005 publications that were considered is posted on the GOLD website. At the January meeting, it was clear that work remaining would permit the report to be finished during the summer of 2006, and the Science Committee requested that, as publications appeared throughout early 2006, they be reviewed carefully for their impact on the recommendations. At the committee's next meeting, in May 2006, publications meeting the search criteria were considered and incorporated into the

current drafts of the chapters where appropriate. A final meeting of the committee was held in September 2006, at which time publications that appeared prior to July 31, 2006 were considered for their impact on the document.

All members of the committee received a summary of citations and all abstracts. Each abstract was assigned to two committee members (members were not assigned papers they had authored), although any member was offered the opportunity to provide an opinion on any abstract. Each member evaluated the assigned abstracts or, where s/he judged necessary, the full publication, by answering specific written questions from a short questionnaire, and indicating whether the scientific data presented affected recommendations in the GOLD report. If so, the member was asked to specifically identify modifications that should be made. The GOLD Science Committee met on a regular basis to discuss each individual publication indicated by at least one member of the committee to have an impact on COPD management, and to reach a consensus on the changes needed in the report. Disagreements were decided by vote.

Periodically throughout the preparation of this report (May and September 2005, May and September 2006), representatives from the GOLD Science Committee met with the GOLD National Leaders to discuss COPD management and issues specific to each of the chapters. The GOLD National Leaders include representatives from over 50 countries and many participated in these interim discussions.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The cost effectiveness of education programs for chronic obstructive pulmonary disease (COPD) is highly dependent on local factors that influence the cost of access to medical services and that will vary substantially between countries. In one cost-benefit analysis of education provided to hospital patients with COPD, an information package resulted in increased knowledge of COPD and reduced use of health services, including reductions of hospital readmissions and general practice consultations. The education package involved training patients to increase knowledge of COPD, medication usage, precautions for exacerbations, and peak flow monitoring technique. However, this study was undertaken in a heterogeneous group of patients - 65% were smokers and 88% were judged to have an asthmatic component to their disease - and these findings may not hold true for a "pure" COPD population. In a study of mild to moderate COPD patients at an out-patient clinic, patient education involving one four-hour group session followed by one to two individual sessions with a nurse and physiotherapist improved patient outcomes and reduced costs in a 12-month follow-up.

The guideline developer reviewed the economic and social burden of COPD: COPD is a costly disease with both direct costs (value of health care resources devoted to diagnosis and medical management) and indirect cots (monetary consequences of disability, missed work, premature mortality, and caregiver or family costs resulting from the illness). In developed countries, exacerbations of COPD account for the greatest burden on the health care system.

Refer to Chapter 2 in the original guideline document for further information about the economic and social burden of COPD.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Periodically throughout the preparation of this report (May and September 2005, May and September 2006), representatives from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Science Committee met with the GOLD National Leaders to discuss chronic obstructive pulmonary disease (COPD) management and issues specific to each of the chapters. The GOLD National Leaders include representatives from over 50 countries and many participated in these interim discussions. In addition, GOLD National Leaders were invited to submit comments on a DRAFT document and their comments were considered by the committee. When the committee completed its work, several other individuals were invited to submit comments on the document as reviewers. The names of reviewers and GOLD National Leaders who submitted comments are in the front material of the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (A-D) are defined at the end of the "Major Recommendations" field.

<u>New Issues Presented in this Report</u>

1. Throughout the document, emphasis has been made that chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation and a range of pathological changes in the lung, some significant extrapulmonary effects, and important comorbidities that may contribute to the severity of the disease in individual patients.
2. In the definition of COPD, the phrase "preventable and treatable" has been incorporated following the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations to recognize the need to present a positive outlook for patients, to encourage the health care community to take a more active role in developing programs for COPD prevention, and to stimulate effective management programs to treat those with the disease.
3. The spirometric classification of severity of COPD now includes four stages—Stage I: Mild; Stage II: Moderate; Stage III: Severe; Stage IV: Very Severe. A fifth category - "Stage 0: At Risk," - that appeared in the 2001 report is no longer included as a stage of COPD, as there is incomplete evidence that the individuals who meet the definition of "At Risk" (chronic cough and sputum production, normal spirometry) necessarily progress on to Stage I. Nevertheless, the importance of the public health message that chronic cough and sputum are not normal is unchanged.

4. The spirometric classification of severity continues to recommend use of the fixed ratio, postbronchodilator forced expiratory volume in one second/forced vital capacity (FEV1/FVC) <0.7, to define airflow limitation. Using the fixed ratio (FEV1/FVC) is particularly problematic in milder patients who are elderly, as the normal process of aging affects lung volumes. Postbronchodilator reference values in this population are urgently needed to avoid potential overdiagnosis.
5. Chapter 2 of the original guideline document, Burden of COPD, provides references to published data from prevalence surveys carried out in a number of countries, using standardized methods and including spirometry, to estimate that about one-quarter of adults aged 40 years and older may have airflow limitation classified as Stage I: Mild COPD or higher. Evidence is also provided that the prevalence of COPD (Stage I: Mild COPD and higher) is appreciably higher in smokers and ex-smokers than in nonsmokers, in those over 40 years than those under 40, and higher in men than in women. The chapter also provides new data on COPD morbidity and mortality.
6. Throughout it is emphasized that cigarette smoke is the most commonly encountered risk factor for COPD and elimination of this risk factor is an important step toward prevention and control of COPD. However, other risk factors for COPD should be taken into account where possible. These include occupational dusts and chemicals, and indoor air pollution from biomass cooking and heating in poorly ventilated dwellings—the latter especially among women in developing countries.
7. Chapter 4 of the original guideline document, Pathology, Pathogenesis, and Pathophysiology, continues with the theme that inhaled cigarette smoke and other noxious particles cause lung inflammation, a normal response which appears to be amplified in patients who develop COPD. The chapter has been considerably updated and revised.
8. Management of COPD continues to be presented in four components: (1) Assess and Monitor Disease; (2) Reduce Risk Factors; (3) Manage Stable COPD; (4) Manage Exacerbations. All components have been updated based on recently published literature. Throughout the document, it is emphasized that the overall approach to managing stable COPD should be individualized to address symptoms and improve quality of life.
9. In Component 4 of the original guideline document, Manage Exacerbations, a COPD exacerbation is defined as: an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.
10. It is widely recognized that a wide spectrum of health care providers are required to assure that COPD is diagnosed accurately, and that individuals who have COPD are treated effectively. The identification of effective health care teams will depend on the local health care system, and much work remains to identify how best to build these health care teams. A chapter on COPD implementation programs and issues for clinical practice has been included but it remains a field that requires considerable attention.

Definition

Spirometric Classification of Severity

For educational reasons, a simple spirometric classification of disease severity into four stages is recommended.

Spirometric Classification of COPD Severity Based on Post-Bronchodilators FEV_1	
Stage I: Mild	$FEV_1/FVC < 0.70$ $FEV_1 \geq 80\%$ predicted
Stage II: Moderate	$FEV_1/FVC < 0.70$ $50\% \leq FEV_1 < 80\%$ predicted
Stage III: Severe	$FEV_1/FVC < 0.70$ $30\% \leq FEV_1 < 50\%$ predicted
Stage IV: Very Severe	$FEV_1/FVC < 0.70$ $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Note: Respiratory failure: arterial partial pressure of oxygen (PaO_2) less than 8.0 kPa (60 mm Hg) with or without arterial partial pressure of CO_2 ($PaCO_2$) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level.

"At Risk for COPD"
A major objective of GOLD is to increase awareness among health care providers and the general public of the significance of COPD symptoms. The classification of severity of COPD now includes four stages classified by spirometry—Stage I: Mild COPD; Stage II: Moderate COPD; Stage III: Severe COPD; Stage IV: Very Severe COPD. A fifth category - "Stage 0: At Risk," – that appeared in the 2001 report is no longer included as a stage of COPD, as there is incomplete evidence that the individuals who meet the definition of "At Risk" (chronic cough and sputum production, normal spirometry) necessarily progress on to Stage I: Mild COPD. Nevertheless, the importance of the public health message that chronic cough and sputum are not normal is unchanged and their presence should trigger a search for underlying cause(s).

Management of COPD

Component 1: Assess and Monitor Disease

Key Points

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry.
- For the diagnosis and assessment of COPD, spirometry is the gold standard as it is the most reproducible, standardized, and objective way of measuring airflow limitation. The presence of a postbronchodilator FEV1/FVC <0.70 and FEV1 <80% predicted confirms the presence of airflow limitation that is not fully reversible.
- Health care workers involved in the diagnosis and management of COPD patients should have access to spirometry.
- Assessment of COPD severity is based on the patient's level of symptoms, the severity of the spirometric abnormality, and the presence of complications.

- Measurement of arterial blood gas tensions should be considered in all patients with FEV1 <50% predicted or clinical signs suggestive of respiratory failure or right heart failure.
- COPD is usually a progressive disease and lung function can be expected to worsen over time, even with the best available care. Symptoms and objective measures of airflow limitation should be monitored to determine when to modify therapy and to identify any complications that may develop.
- Comorbidities are common in COPD and should be actively identified. Comorbidities often complicate the management of COPD, and vice versa.

Initial Diagnosis

A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease. The diagnosis should be confirmed by spirometry. The presence of a postbronchodilator FEV_1/FVC <0.70 and FEV_1 < 80% predicted confirms the presence of airflow limitation that is not fully reversible.

Key Indicators for Considering a Diagnosis of COPD	
Consider COPD, and perform spirometry, if any of these indicators are present in an individual over age 40. These indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of a diagnosis of COPD. Spirometry is needed to establish a diagnosis of COPD.	
Dyspnea that is:	Progressive (worsens over time) Usually worse with exercise Persistent (present every day) Described by the patient as an "increased effort to breathe," "heaviness," "air hunger," or "gasping."
Chronic Cough	May be intermittent and may be unproductive
Chronic sputum production:	Any pattern of chronic sputum production may indicate COPD.
History of exposure to risk factors, especially:	Tobacco smoke. Occupational dusts and chemicals Smoke from home cooking and heating fuels.

See the original guideline document for a discussion of common symptoms, including dyspnea, cough, sputum production, wheezing and chest tightness, and other features of severe disease.

Medical History

A detailed medical history of a new patient known or thought to have COPD should assess:

- Patient's exposure to risk factors, such as smoking and occupational or environmental exposures
- Past medical history, including asthma, allergy, sinusitis, or nasal polyps; respiratory infections in childhood; other respiratory diseases
- Family history of COPD or other chronic respiratory disease
- Pattern of symptom development: COPD typically develops in adult life and most patients are conscious of increased breathlessness, more frequent

"winter colds," and some social restriction for a number of years before seeking medical help.
- History of exacerbations or previous hospitalizations for respiratory disorder: Patients may be aware of periodic worsening of symptoms even if these episodes have not been identified as exacerbations of COPD.
- Presence of comorbidities, such as heart disease, malignancies, osteoporosis, and musculoskeletal disorders, which may also contribute to restriction of activity.
- Appropriateness of current medical treatments: For example, beta-blockers commonly prescribed for heart disease are usually contraindicated in COPD.
- Impact of disease on patient's life, including limitation of activity, missed work and economic impact, effect on family routines, feelings of depression or anxiety
- Social and family support available to the patient
- Possibilities for reducing risk factors, especially smoking cessation

Physical Examination

Though an important part of patient care, a physical examination is rarely diagnostic in COPD. Physical signs of airflow limitation are usually not present until significant impairment of lung function has occurred and their detection has a relatively low sensitivity and specificity. A number of physical signs may be present in COPD, but their absence does not exclude the diagnosis.

Refer to the original guideline document for specific physical examination assessments.

Measurement of Airflow Limitation (Spirometry)

Spirometry should be undertaken in all patients who may have COPD. It is needed to make a confident diagnosis of COPD and to exclude other diagnoses that may present with similar symptoms. Although spirometry does not fully capture the impact of COPD on a patient's health, it remains the gold standard for diagnosing the disease and monitoring its progression. It is the best standardized, most reproducible, and most objective measurement of airflow limitation available. Good quality spirometric measurement is possible and all health care workers who care for COPD patients should have access to spirometry. Figure 5.1-4 in the original guideline document summarizes some of the factors needed to achieve accurate test results.

Spirometry should measure the volume of air forcibly exhaled from the point of maximal inspiration (forced vital capacity, FVC) and the volume of air exhaled during the first second of this maneuver (forced expiratory volume in one second, FEV_1), and the ratio of these two measurements (FEV_1/FVC) should be calculated. Spirometry measurements are evaluated by comparison with reference values based on age, height, sex, and race (use appropriate reference values).

Assessment of COPD Severity

Assessment of COPD severity is based on the patient's level of symptoms, the severity of the spirometric abnormality, and the presence of complications such as respiratory failure, right heart failure, weight loss, and arterial hypoxemia.

When evaluating symptomatic patients presenting to a physician, the severity of the patient's symptoms and the degree to which they affect his or her daily life, not just the severity of airflow obstruction, are the major determinants of health status. The severity of a patient's breathlessness is important and can be usefully gauged by the Medical Research Council (MRC) scale (see Figure 5.1-2 in the original guideline document).

Objectively measured exercise impairment, assessed by a reduction in self-paced walking distance or during incremental exercise testing in a laboratory, is a powerful indicator of health status impairment and predictor of prognosis. The ratio of inspiratory capacity to total lung capacity determined plethysmographically has also been found to be prognostically useful. Similarly, weight loss and reduction in the arterial oxygen tension identify patients at increased risk for mortality.

A relatively simple approach to identifying disease severity using a combination of most of the above variables has been proposed. The BODE method gives a composite score (Body mass index, Obstruction, Dyspnea, and Exercise) that is a better predictor of subsequent survival than any component singly, and its properties as a measurement tool are under investigation.

Refer to the original guideline document for additional investigations that are considered.

Differential Diagnosis

In some patients with chronic asthma, a clear distinction from COPD is not possible using current imaging and physiological testing techniques, and it is assumed that asthma and COPD coexist in these patients. In these cases, current management is similar to that of asthma. Other potential diagnoses are usually easier to distinguish from COPD. Refer to Figure 5.1-7 in the original guideline document for other potential diagnoses.

Ongoing Monitoring and Assessment

Visits to health care facilities will increase in frequency as COPD progresses. The type of health care workers seen, and the frequency of visits, will depend on the health care system. Ongoing monitoring and assessment in COPD ensures that the goals of treatment are being met and should include evaluation of: (1) exposure to risk factors, especially tobacco smoke; (2) disease progression and development of complications; (3) pharmacotherapy and other medical treatment; (4) exacerbation history; (5) comorbidities.

Suggested questions for follow-up visits are listed in Figure 5.1-8 in the original guideline document. The best way to detect changes in symptoms and overall health status is to ask the patient the same questions at each visit.

Monitor Disease Progression and Development of Complications

COPD is usually a progressive disease. Lung function can be expected to worsen over time, even with the best available care. Symptoms and objective measures

of airflow limitation should be monitored to determine when to modify therapy and to identify any complications that may develop. As at the initial assessment, follow-up visits should include a physical examination and discussion of symptoms, particularly any new or worsening symptoms.

Pulmonary Function

A patient's decline in lung function is best tracked by periodic spirometry measurements although useful information about lung function decline is unlikely from spirometry measurements performed more than once a year. Spirometry should be performed if there is a substantial increase in symptoms or a complication.

Other pulmonary function tests, such as flow-volume loops, diffusing capacity (D_{LCO}) measurements, inspiratory capacity, and measurement of lung volumes are not needed in a routine assessment but can provide information about the overall impact of the disease and can be valuable in resolving diagnostic uncertainties and assessing patients for surgery.

Refer to the original guideline document for other specific assessments of disease progression.

Monitor Pharmacotherapy and Other Medical Treatment

In order to adjust therapy appropriately as the disease progresses, each follow-up visit should include a discussion of the current therapeutic regimen. Dosages of various medications, adherence to the regimen, inhaler technique, effectiveness of the current regime at controlling symptoms, and side effects of treatment should be monitored.

Monitor Exacerbation History

During periodic assessments, health care workers should question the patient and evaluate any records of exacerbations, both self-treated and those treated by other health care providers. Frequency, severity, and likely causes of exacerbations should be evaluated. Increased sputum volume, acutely worsening dyspnea, and the presence of purulent sputum should be noted. Specific inquiry into unscheduled visits to providers, telephone calls for assistance, and use of urgent or emergency care facilities may be helpful. Severity can be estimated by the increased need for bronchodilator medication or glucocorticosteroids and by the need for antibiotic treatment. Hospitalizations should be documented, including the facility, duration of stay, and any use of critical care or intubation. The clinician then can request summaries of all care received to facilitate continuity of care.

Monitor Comorbidities

Comorbidities are common in COPD. Some may be an indirect result of COPD, arising independently but more likely to occur when COPD is present, e.g., ischemic heart disease, bronchial carcinoma, osteoporosis. Other comorbid conditions may coexist with COPD because they become prevalent as part of the

aging process, e.g., arthritis, diabetes, reflux esophagitis. All comorbid conditions become harder to manage when COPD is present, either because COPD adds to the total level of disability or because COPD therapy adversely affects the comorbid disorder. All comorbid conditions amplify the disability associated with COPD and can potentially complicate its management. Until more integrated guidance about disease management for specific comorbid problems becomes available, the focus should be on identification and management of these individual problems in line with local treatment guidance.

Component 2: Reduce Risk Factors

Key Points

- Reduction of total personal exposure to tobacco smoke, occupational dusts and chemicals, and indoor and outdoor air pollutants are important goals to prevent the onset and progression of COPD.
- Smoking cessation is the single most effective—and cost effective—intervention in most people to reduce the risk of developing COPD and stop its progression (Evidence A).
- Comprehensive tobacco control policies and programs with clear, consistent, and repeated nonsmoking messages should be delivered through every feasible channel.
- Efforts to reduce smoking through public health initiatives should also focus on passive smoking to minimize risks for nonsmokers.
- Many occupationally induced respiratory disorders can be reduced or controlled through a variety of strategies aimed at reducing the burden of inhaled particles and gases.
- Reducing the risk from indoor and outdoor air pollution is feasible and requires a combination of public policy and protective steps taken by individual patients.

Introduction

Identification, reduction, and control of risk factors are important steps toward prevention and treatment of any disease. In the case of COPD, these factors include tobacco smoke, occupational exposures, and indoor and outdoor air pollution and irritants. Since cigarette smoking is the most commonly encountered risk factor for COPD worldwide, tobacco control (smoking prevention) programs should be implemented and smoking cessation programs should be readily available and encouraged for all individuals who smoke. Reduction of total personal exposure to occupational dusts, fumes, and gases and to indoor and outdoor air pollutants is also an important goal to prevent the onset and progression of COPD.

Tobacco Smoke

Smoking Prevention

Comprehensive tobacco control policies and programs with clear, consistent, and repeated nonsmoking messages should be delivered through every feasible channel, including health care providers, community activities, schools, and radio, television, and print media. National and local campaigns should be undertaken to

reduce exposure to tobacco smoke in public forums. Such bans are proving to be workable and to result in measurable gains in respiratory health. Legislation to establish smoke-free schools, public facilities, and work environments should be developed and implemented by government officials and public health workers, and encouraged by the public. Smoking prevention programs should target all ages, including young children, adolescents, young adults, and pregnant women. Interventions to prevent smoking uptake and maximize cessation should be implemented at every level of the health care system. Physicians and public health officials should encourage smoke-free homes.

Smoking Cessation

Smoking cessation is the single most effective—and cost effective—way to reduce exposure to COPD risk factors. Quitting smoking can prevent or delay the development of airflow limitation, or reduce its progression, and can have a substantial effect on subsequent mortality. All smokers—including those who may be at risk for COPD as well as those who already have the disease—should be offered the most intensive smoking cessation intervention feasible.

The Role of Health Care Providers in Smoking Cessation

A successful smoking cessation strategy requires a multifaceted approach, including public policy, information dissemination programs, and health education through the media and schools. However, health care providers, including physicians, nurses, dentists, psychologists, pharmacists, and others, are key to the delivery of smoking cessation messages and interventions. Involving as many of these individuals as possible will help. Health care workers should encourage all patients who smoke to quit, even those patients who come to the health care provider for unrelated reasons and do not have symptoms of COPD, evidence of airflow limitation, or other smoking-related disease. Guidelines for smoking cessation entitled Treating Tobacco Use and Dependence: A Clinical Practice Guideline were published by the US Public Health Service. The major conclusions are summarized in Figure 5.2-2 in the original guideline document. See also Figure 5.2-3 in the original guideline document fort brief strategies to help the patient willing to quit.

Counseling

Counseling delivered by physicians and other health professionals significantly increases quit rates over self-initiated strategies. Even a brief (3-minute) period of counseling to urge a smoker to quit results in smoking cessation rates of 5-10%. At the very least, this should be done for every smoker at every health care provider visit. Education in how to offer optimal smoking cessation advice and support should be a mandatory element of curricula for health professionals.

Pharmacotherapy

Numerous effective pharmacotherapies for smoking cessation now exist, and pharmacotherapy is recommended when counseling is not sufficient to help patients quit smoking. Special consideration should be given before using pharmacotherapy in selected populations: people with medical contraindications,

light smokers (fewer than 10 cigarettes/day), and pregnant and adolescent smokers.

Refer to the original guideline document for information on nicotine replacement products and other pharmacotherapies.

Occupational Exposures

Although it is not known how many individuals are at risk of developing respiratory disease from occupational exposures in either developing or developed countries, many occupationally induced respiratory disorders can be reduced or controlled through a variety of strategies aimed at reducing the burden of inhaled particles and gases:

- Implement, monitor, and enforce strict, legally mandated control of airborne exposure in the workplace.
- Initiate intensive and continuing education of exposed workers, industrial managers, health care workers, primary care physicians, and legislators.
- Educate employers, workers, and policymakers on how cigarette smoking aggravates occupational lung diseases and why efforts to reduce smoking where a hazard exists are important.

The main emphasis should be on primary prevention, which is best achieved by the elimination or reduction of exposures to various substances in the workplace. Secondary prevention, achieved through surveillance and early case detection, is also of great importance. Both approaches are necessary to improve the present situation and to reduce the burden of lung disease. Although studies as yet have not been done to demonstrate reduced burden of disease, it is the logical consequence of effective strategies to reduce workplace exposure to respiratory irritants and toxic inhalants.

Indoor and Outdoor Air Pollution

Individuals experience diverse indoor and outdoor environments throughout the day, each of which has its own unique set of air contaminants and particulates that cause adverse effects on lung function.

Although outdoor and indoor air pollution are generally considered separately, the concept of total personal exposure may be more relevant for COPD. Reducing the risk from indoor and outdoor air pollution is feasible and requires a combination of public policy and protective steps taken by individual patients. Reduction of exposure to smoke from biomass fuel, particularly among women and children, is a crucial goal to reduce the prevalence of COPD worldwide. Although efficient non-polluting cooking stoves have been developed, their adoption has been slow due to social customs and cost.

Regulation of Air Quality

At the national level, achieving a set level of air quality standards should be a high priority; this goal will normally require legislative action. Details on setting and maintaining air quality goals are beyond the scope of this document, but public

policy to reduce vehicle and industrial emissions to safe levels is an urgent priority to reduce the development of COPD as well as symptoms, exacerbations, and hospital admissions in those with disease. Understanding health risks posed by local air pollution sources may be difficult and requires skills in community health, toxicology, and epidemiology. Local physicians may become involved through concerns about the health of their patients or as advocates for the community's environment.

Steps for Health Care Providers/Patients

The health care provider should consider COPD risk factors including smoking history, family history, exposure to indoor/outdoor pollution) and socioeconomic status for each individual patient. Some steps to consider:

Individuals at risk for COPD:

- Patients should be counseled concerning the nature and degree of their risk for COPD.
- If various solid fuels are used for cooking and heating, adequate ventilation should be encouraged.
- Respiratory protective equipment has been developed for use in the workplace in order to minimize exposure to toxic gases and particles. Under most circumstances, vigorous attempts should be made to reduce exposure through reducing workplace emissions and improving ventilation measures, rather than simply by using respiratory protection to reduce the risks of ambient air pollution.
- Ventilation and interventions to meet safe air quality standards in the workplace offer the greatest opportunity to reduce worker exposure to known atmospheric pollutants and reduce the risk of developing COPD, although to date there are no studies to quantify these benefits.

Patients who have been diagnosed with COPD:

- Persons with advanced COPD should monitor public announcements of air quality and be aware that staying indoors when air quality is poor may help reduce their symptoms.
- The use of medication should follow the usual clinical indications; therapeutic regimens should not be adjusted because of the occurrence of a pollution episode without evidence of worsening of symptoms or lung function.
- Those who are at high risk should avoid vigorous exercise outdoors during pollution episodes.
- Air cleaners have not been shown to have health benefits, whether directed at pollutants generated by indoor sources or at those brought in with outdoor air.

Component 3: Manage Stable COPD

Key Points

- The overall approach to managing stable COPD should be individualized to address symptoms and improve quality of life.

- For patients with COPD, health education plays an important role in smoking cessation (Evidence A) and can also play a role in improving skills, ability to cope with illness and health status.
- None of the existing medications for COPD have been shown to modify the long-term decline in lung function that is the hallmark of this disease (Evidence A). Therefore, pharmacotherapy for COPD is used to decrease symptoms and/or complications.
- Bronchodilator medications are central to the symptomatic management of COPD (Evidence A). They are given on an as-needed basis or on a regular basis to prevent or reduce symptoms and exacerbations.
- The principal bronchodilator treatments are $beta_2$-agonists, anticholinergics, and methylxanthines used singly or in combination (Evidence A).
- Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators (Evidence A).
- The addition of regular treatment with inhaled glucocorticosteroids to bronchodilator treatment is appropriate for symptomatic COPD patients with an FEV_1 <50% predicted (Stage III: Severe COPD and Stage IV: Very Severe COPD) and repeated exacerbations (Evidence A).
- Chronic treatment with systemic glucocorticosteroids should be avoided because of an unfavorable benefit-to-risk ratio (Evidence A).
- In COPD patients influenza vaccines can reduce serious illness (Evidence A). Pneumococcal polysaccharide vaccine is recommended for COPD patients 65 years and older and for COPD patients younger than age 65 with an FEV_1 <40% predicted (Evidence B).
- All COPD patients benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue (Evidence A).
- The long-term administration of oxygen (>15 hours per day) to patients with chronic respiratory failure has been shown to increase survival (Evidence A).

Introduction

The overall approach to managing stable COPD should be characterized by an increase in treatment, depending on the severity of the disease and the clinical status of the patient. The step-down approach used in the chronic treatment of asthma is not applicable to COPD since COPD is usually stable and very often progressive. Management of COPD involves several objectives (see Chapter 5, Introduction in the original guideline document) that should be met with minimal side effects from treatment. It is based on an individualized assessment of disease severity and response to various therapies. Refer to Figure 5.3-1 in the original guideline document for factors that affect the severity of COPD.

The classification of severity of stable COPD incorporates an individualized assessment of disease severity and therapeutic response into the management strategy. The severity of airflow limitation (see Figure 1-2 in the original guideline document) provides a general guide to the use of some treatments, but the selection of therapy is predominantly determined by the patient's symptoms and clinical presentation. Treatment also depends on the patient's educational level and willingness to apply the recommended management, on cultural and local conditions, and on the availability of medications.

Education

Although patient education is generally regarded as an essential component of care for any chronic disease, the role of education in COPD has been poorly studied. Assessment of the value of education in COPD may be difficult because of the relatively long time required to achieve improvements in objective measurements of lung function.

Ideally, educational messages should be incorporated into all aspects of care for COPD and may take place in many settings: consultations with physicians or other health care workers, home-care or outreach programs, and comprehensive pulmonary rehabilitation programs.

Goals and Educational Strategies

It is vital for patients with COPD to understand the nature of their disease, risk factors for progression, and their role and the role of health care workers in achieving optimal management and health outcomes. Education should be tailored to the needs and environment of the individual patient, interactive, directed at improving quality of life, simple to follow, practical, and appropriate to the intellectual and social skills of the patient and the caregivers.

In managing COPD, open communication between patient and physician is essential. In addition to being empathic, attentive and communicative, health professionals should pay attention to patients' fears and apprehensions, focus on educational goals, tailor treatment regimens to each individual patient, anticipate the effect of functional decline, and optimize patients' practical skills.

Several specific education strategies have been shown to improve patient adherence to medication and management regimens. In COPD, adherence does not simply refer to whether patients take their medication appropriately. It also covers a range of nonpharmacologic treatments, e.g., maintaining an exercise program after pulmonary rehabilitation, undertaking and sustaining smoking cessation, and using devices such as nebulizers, spacers, and oxygen concentrators properly.

Components of an Education Program

The topics that seem most appropriate for an education program include smoking cessation; basic information about COPD and pathophysiology of the disease; general approach to therapy and specific aspects of medical treatment; self-management skills; strategies to help minimize dyspnea; advice about when to seek help; self-management and decision-making during exacerbations; and advance directives and end-of-life issues (See Table below). Education should be part of consultations with health care workers beginning at the time of first assessment for COPD and continuing with each follow-up visit. The intensity and content of these educational messages should vary depending on the severity of the patient's disease. In practice, a patient often poses a series of questions to the physician (see Figure 5.3-3 in the original guideline document). It is important to answer these questions fully and clearly, as this may help make treatment more effective.

Topics of Patient Education

Topics of Patient Education
For all patients: • Information and advice about reducing risk factors Stage I: Mild COPD through Stage III: Severe COPD Above topic, plus: • Information about the nature of COPD • Instruction on how to use inhalers and other treatments • Recognition and treatment of exacerbations • Strategies for minimizing dyspnea Stage IV: Very Severe COPD Above topics, plus: • Information about complications • Information about oxygen treatment • Advance directives and end-of-life decisions

There are several different types of educational programs, ranging from simple distribution of printed materials, to teaching sessions designed to convey information about COPD, to workshops designed to train patients in specific skills (e.g., self-management). In general, case-management approaches to medical problems have been somewhat disappointing. However, COPD patients recruited to a comprehensive COPD education program in Canada had significantly fewer exacerbations and hospitalizations and used fewer health care resources. These encouraging results require replication in other health care systems and patient groups.

Although printed materials may be a useful adjunct to other educational messages, passive dissemination of printed materials alone does not improve skills or health outcomes. Education is most effective when it is interactive and conducted in small workshops (Evidence B) designed to improve both knowledge and skills. Behavioral approaches such as cognitive therapy and behavior modification lead to more effective self-management skills and maintenance of exercise programs.

Pharmacologic Treatment

Overview of the Medications

Pharmacologic therapy is used to prevent and control symptoms, reduce the frequency and severity of exacerbations, improve health status, and improve exercise tolerance. None of the existing medications for COPD have been shown to modify the long-term decline in lung function that is the hallmark of this disease (Evidence A). However, this should not preclude efforts to use medications to control symptoms. Since COPD is usually progressive,

recommendations for the pharmacological treatment of COPD reflect the following general principles:

- Treatment tends to be cumulative with more medications being required as the disease state worsens.
- Regular treatment needs to be maintained at the same level for long periods of time unless significant side effects occur or the disease worsens.
- Individuals differ in their response to treatment and in the side effects they report during therapy. Careful monitoring is needed over an appropriate period to ensure that the specific aim of introducing a therapy has been met without an unacceptable cost to the patient. The effect of therapy in COPD may occur sooner after treatment with bronchodilators and inhaled glucocorticosteroids than previously thought, although at present, there is no effective way to predict whether or not treatment will reduce exacerbations.

The medications are presented in the order in which they would normally be introduced in patient care, based on the level of disease severity and clinical symptoms. However, each treatment regimen needs to be patient-specific as the relationship between the severity of symptoms and the severity of airflow limitation is influenced by other factors, such as the frequency and severity of exacerbations, the presence of one or more complications, the presence of respiratory failure, comorbidities (cardiovascular disease, sleep-related disorders, etc.), and general health status.

The classes of medications commonly used in treating COPD are shown in Figure 5.3-4 in the original guideline document. The choice within each class depends on the availability of medication and the patient's response.

Bronchodilators

Bronchodilator medications are central to the symptomatic management of COPD (Evidence A) (see Table below). They are given either on an as-needed basis for relief of persistent or worsening symptoms, or on a regular basis to prevent or reduce symptoms. The side effects of bronchodilator therapy are pharmacologically predictable and dose dependent. Adverse effects are less likely, and resolve more rapidly after treatment withdrawal, with inhaled than with oral treatment. However, COPD patients tend to be older than asthma patients and more likely to have comorbidities, so their risk of developing side effects is greater.

Bronchodilators in Stable COPD
• Bronchodilator medications are central to symptom management in COPD. • Inhaled therapy is preferred. • The choice between beta$_2$-agonist, anticholinergic, theophylline, or combination therapy depends on availability and individual response in terms of symptom relief and side effects. • Bronchodilators are prescribed on an as-needed or on a regular basis to prevent or reduce symptoms. • Long-acting inhaled bronchodilators are more effective and convenient. • Combining bronchodilators may improve efficacy and decrease the risk of side

effects compared to increasing the dose of a single bronchodilator.

See the original guideline document for more information on bronchodilators, including $beta_2$-agonists, anticholinergics, methylxanthines, and combination bronchodilator therapy.

Glucocorticosteroids

The effects of oral and inhaled glucocorticosteroids in COPD are much less dramatic than in asthma, and their role in the management of stable COPD is limited to specific indications. The use of glucocorticosteroids for the treatment of acute exacerbations is described in the section "Component 4: Manage Exacerbations."

See the original guideline document for a discussion of the use of oral and inhaled glucocorticosteroids in the management of chronic COPD.

Pharmacologic Therapy by Disease Severity

Figure 5.3-7 in the original guideline documents provides a summary of recommended treatment at each stage of COPD. For patients with few or intermittent symptoms (Stage I: Mild COPD), use of a short-acting inhaled bronchodilator as needed to control dyspnea is sufficient. If inhaled bronchodilators are not available, regular treatment with slow-release theophylline should be considered.

In patients with Stage II: Moderate COPD to Stage IV: Very Severe COPD whose dyspnea during daily activities is not relieved despite treatment with as-needed short-acting bronchodilators, adding regular treatment with a long-acting inhaled bronchodilator is recommended (Evidence A). Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting bronchodilators (Evidence A). There is insufficient evidence to favor one long-acting bronchodilator over others. For patients on regular long-acting bronchodilator therapy who need additional symptom control, adding theophylline may produce additional benefits (Evidence B).

Patients with Stage II: Moderate COPD to Stage IV: Very Severe COPD who are on regular short- or long-acting bronchodilator therapy may also use a short-acting bronchodilator as needed.

Some patients may request regular treatment with high-dose nebulized bronchodilators, especially if they have experienced subjective benefit from this treatment during an acute exacerbation. Clear scientific evidence for this approach is lacking, but one suggested option is to examine the improvement in mean daily peak expiratory flow recording during two weeks of treatment in the home and continue with nebulizer therapy if a significant change occurs. In general, nebulized therapy for a stable patient is not appropriate unless it has been shown to be better than conventional dose therapy.

In patients with a postbronchodilator FEV_1 <50% predicted (Stage III: Severe COPD to Stage IV: Very Severe COPD) and a history of repeated exacerbations (for example, 3 in the last 3 years), regular treatment with inhaled glucocorticosteroids reduces the frequency of exacerbations and improves health status. In these patients, regular treatment with an inhaled glucocorticosteroid should be added to long-acting inhaled bronchodilators. Chronic treatment with oral glucocorticosteroids should be avoided.

Refer to the original guideline document for a discussion of other pharmacologic treatments.

Non-Pharmacologic Treatment

Rehabilitation

The principal goals of pulmonary rehabilitation are to reduce symptoms, improve quality of life, and increase physical and emotional participation in everyday activities. To accomplish these goals, pulmonary rehabilitation covers a range of non-pulmonary problems that may not be adequately addressed by medical therapy for COPD. Such problems, which especially affect patients with Stage II: Moderate COPD, Stage III: Severe COPD, and Stage IV: Very Severe COPD, include exercise de-conditioning, relative social isolation, altered mood states (especially depression), muscle wasting, and weight loss. These problems have complex interrelationships and improvement in any one of these interlinked processes can interrupt the "vicious circle" in COPD so that positive gains occur in all aspects of the illness (see Figure 5.3-9 in the original guideline document). A comprehensive statement on pulmonary rehabilitation has been prepared by the American Thoracic Society/European Respiratory Society.

See Figure 5.3-10 in the original guideline document for a list of benefits of pulmonary rehabilitation in COPD.

Patient Selection and Program Design

Although more information is needed on criteria for patient selection for pulmonary rehabilitation programs, COPD patients at all stages of disease appear to benefit from exercise training programs, improving with respect to both exercise tolerance and symptoms of dyspnea and fatigue (Evidence A). Data suggest that these benefits can be sustained even after a single pulmonary rehabilitation program.

Benefit does wane after a rehabilitation program ends, but if exercise training is maintained at home, the patient's health status remains above pre-rehabilitation levels (Evidence B). To date there is no consensus on whether repeated rehabilitation courses enable patients to sustain the benefits gained through the initial course.

Ideally, pulmonary rehabilitation should involve several types of health professionals. Significant benefits can also occur with more limited personnel, as long as dedicated professionals are aware of the needs of each patient. Benefits have been reported from rehabilitation programs conducted in inpatient,

outpatient, and home settings. Considerations of cost and availability most often determine the choice of setting. The educational and exercise training components of rehabilitation are usually conducted in groups, normally with 6 to 8 individuals per class (Evidence D).

Refer to the original guideline document for considerations important in choosing patients.

Components of Pulmonary Rehabilitation Programs

The components of pulmonary rehabilitation vary widely from program to program but a comprehensive pulmonary rehabilitation program includes exercise raining, nutrition counseling, and education. See the original guideline document for a discussion of these components.

Assessment and Follow-up

Baseline and outcome assessments of each participant in a pulmonary rehabilitation program should be made to quantify individual gains and target areas for improvement. Assessments should include:

- Detailed history and physical examination
- Measurement of spirometry before and after a bronchodilator drug
- Assessment of exercise capacity
- Measurement of health status and impact of breathlessness
- Assessment of inspiratory and expiratory muscle strength and lower limb strength (e.g., quadriceps) in patients who suffer from muscle wasting

The first two assessments are important for establishing entry suitability and baseline status but are not used in outcome assessment. The last three assessments are baseline and outcome measures.

Oxygen Therapy

Oxygen therapy, one of the principal nonpharmacologic treatments for patients with Stage IV: Very Severe COPD, can be administered in three ways: long-term continuous therapy, during exercise, and to relieve acute dyspnea. The primary goal of oxygen therapy is to increase the baseline PaO_2 to at least 8.0 kPa (60 mm Hg) at sea level and rest, and/or produce an SaO_2 at least 90%, which will preserve vital organ function by ensuring adequate delivery of oxygen.

The long-term administration of oxygen (>15 hours per day) to patients with chronic respiratory failure has been shown to increase survival. It can also have a beneficial impact on hemodynamics, hematologic characteristics, exercise capacity, lung mechanics, and mental state. Continuous oxygen therapy decreased resting pulmonary artery pressure in one study but not in another study. Prospective studies have shown that the primary hemodynamic effect of oxygen therapy is preventing the progression of pulmonary hypertension. Long-term oxygen therapy improves general alertness, motor speed, and hand grip, although the data are less clear about changes in quality of life and emotional state. The possibility of walking while using some oxygen devices may help to

improve physical conditioning and have a beneficial influence on the psychological state of patients.

Long-term oxygen therapy is generally introduced in Stage IV: Very Severe COPD for patients who have:

- PaO_2 at or below 7.3 kPa (55 mm Hg) or SaO_2 at or below 88%, with or without hypercapnia (Evidence B); or
- PaO_2 between 7.3 kPa (55 mm Hg) and 8.0 kPa (60 mm Hg), or SaO2 of 88%, if there is evidence of pulmonary hypertension, peripheral edema suggesting congestive cardiac failure, or polycythemia (hematocrit >55%) (Evidence D).

A decision about the use of long-term oxygen should be based on the waking PaO_2 values. The prescription should always include the source of supplemental oxygen (gas or liquid), method of delivery, duration of use, and flow rate at rest, during exercise, and during sleep. A detailed review of the uses of oxygen in COPD, together with possible assessment algorithms and information about methods of delivery, is available from http://www.thoracic.org/.

Refer to the original guideline document for a more details about oxygen therapy, including oxygen use in air travel.

Ventilatory Support

Noninvasive ventilation (using either negative or positive pressure devices) is now widely used to treat acute exacerbations of COPD (see Component 4). Negative pressure ventilation is not indicated for the chronic management of Stage IV: Very Severe COPD patients, with or without CO_2 retention. It has been demonstrated to have no effect on shortness of breath, exercise tolerance, arterial blood gases, respiratory muscle strength, or quality of life in a large randomized trial in COPD patients with chronic respiratory failure.

Although preliminary studies suggested that combining noninvasive intermittent positive pressure ventilation (NIPPV) with long-term oxygen therapy could improve some outcome variables, current data do not support the routine use of this combination. However, compared with long-term oxygen therapy alone, the addition of NIPPV can lessen carbon dioxide retention and improve shortness of breath in some patients. Thus, although at present long-term NIPPV cannot be recommended for the routine treatment of patients with chronic respiratory failure due to COPD, the combination of NIPPV with long-term oxygen therapy may be of some use in a selected subset of patients, particularly in those with pronounced daytime hypercapnia.

Surgical Treatments

Bullectomy

Bullectomy is an older surgical procedure for bullous emphysema. Removal of a large bulla that does not contribute to gas exchange decompresses the adjacent lung parenchyma. Bullectomy can be performed thoracoscopically. In carefully

selected patients, this procedure is effective in reducing dyspnea and improving lung function (Evidence C).

Lung Volume Reduction Surgery (LVRS)

LVRS is a surgical procedure in which parts of the lung are resected to reduce hyperinflation, making respiratory muscles more effective pressure generators by improving their mechanical efficiency (as measured by length/tension relationship, curvature of the diaphragm, and area of apposition). In addition, LVRS increases the elastic recoil pressure of the lung and thus improves expiratory flow rates.

Although the results of the large multicenter study showed some very positive results of surgery in a select group of patients, LVRS is an expensive palliative surgical procedure and can be recommended only in carefully selected patients.

Lung Transplantation

In appropriately selected patients with very advanced COPD, lung transplantation has been shown to improve quality of life and functional capacity (Evidence C), although the Joint United Network for Organ Sharing in 1998 found that lung transplantation does not confer a survival benefit in patients with end-stage emphysema after two years. Criteria for referral for lung transplantation include FEV_1 <35% predicted, PaO_2 <7.3 to 8.0 kPa (55 to 60 mm Hg), $PaCO_2$ >6.7 kPa (50 mm Hg), and secondary pulmonary hypertension.

Refer to the original guideline document for special considerations.

Component 4: Manage Exacerbations

- An exacerbation of COPD is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.
- The most common causes of an exacerbation are infection of the tracheobronchial tree and air pollution, but the cause of about one-third of severe exacerbations cannot be identified (Evidence B).
- Inhaled bronchodilators (particularly inhaled $beta_2$-agonists with or without anticholinergics) and oral glucocorticosteroids are effective treatments for exacerbations of COPD (Evidence A).
- Patients experiencing COPD exacerbations with clinical signs of airway infection (e.g., increased sputum purulence) may benefit from antibiotic treatment (Evidence B).
- Noninvasive mechanical ventilation in exacerbations improves respiratory acidosis, increases pH, decreases the need for endotracheal intubation, and reduces $PaCO_2$, respiratory rate, severity of breathlessness, the length of hospital stay, and mortality (Evidence A).
- Medications and education to help prevent future exacerbations should be considered as part of follow-up, as exacerbations affect the quality of life and prognosis of patients with COPD.

Introduction

COPD is often associated with exacerbations of symptoms. An exacerbation of COPD is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD. Exacerbations are categorized in terms of either clinical presentation (number of symptoms) and/or heath-care resources utilization. The impact of exacerbations is significant and a patient's symptoms and lung function may both take several weeks to recover to the baseline values.

Diagnosis and Assessment of Severity

Medical History

Increased breathlessness, the main symptom of an exacerbation, is often accompanied by wheezing and chest tightness, increased cough and sputum, change of the color and/or tenacity of sputum, and fever.

Exacerbations may also be accompanied by a number of nonspecific complaints, such as tachycardia and tachypnea, malaise, insomnia, sleepiness, fatigue, depression, and confusion. A decrease in exercise tolerance, fever, and/or new radiological anomalies suggestive of pulmonary disease may herald a COPD exacerbation. An increase in sputum volume and purulence points to a bacterial cause, as does prior history of chronic sputum production.

Assessment of Severity

Assessment of the severity of an exacerbation is based on the patient's medical history before the exacerbation, preexisting comorbidities, symptoms, physical examination, arterial blood gas measurements, and other laboratory tests (see Table below). Specific information is required on the frequency and severity of attacks of breathlessness and cough, sputum volume and color, and limitation of daily activities. When available, prior arterial blood gas measurements are extremely useful for comparison with those made during the acute episode, as an acute change in these tests is more important than their absolute values. Thus, where possible, physicians should instruct their patients to bring the summary of their last evaluation when they come to the hospital with an exacerbation. In patients with Stage IV: Very Severe COPD, the most important sign of a severe exacerbation is a change in the mental status of the patient and this signals a need for immediate evaluation in the hospital.

Assessment of COPD Exacerbations: Medical History and Signs of Severity	
Medical History	Signs of Severity
• Severity of FEV_1 • Duration of worsening or new symptoms • Number of previous episodes (exacerbations/hospitalizations) • Comorbidities	• Use of accessory respiratory muscles • Paradoxical chest wall movements • Worsening or new onset central cyanosis

Assessment of COPD Exacerbations: Medical History and Signs of Severity	
Medical History	Signs of Severity
• Present treatment regimen	• Development of peripheral edema • Hemodynamic instability • Signs of right heart failure • Reduced alertness

Refer to the original guideline document for a discussion of methods of assessing severity, including spirometry, pulse oximetry and arterial blood gas measurement, chest x-ray and electrocardiogram (ECG), and other laboratory tests.

Differential Diagnosis

Ten to 30% of patients with apparent exacerbations of COPD do not respond to treatment. In such cases the patient should be re-evaluated for other medical conditions that can aggravate symptoms or mimic COPD exacerbations. These conditions include pneumonia, congestive heart failure, pneumothorax, pleural effusion, pulmonary embolism, and cardiac arrhythmia. Noncompliance with the prescribed medication regimen can also cause increased symptoms that may be confused with a true exacerbation. Elevated serum levels of brain-type natriuretic peptide, in conjunction with other clinical information, identifies patients with acute dyspnea secondary to congestive heart failure and enables them to be distinguished from patients with COPD exacerbations.

Home Management

There is increasing interest in home care for end-stage COPD patients, although economic studies of home-care services have yielded mixed results.

The algorithm reported in Figure 5.4-2 in the original guideline document may assist in the management of an exacerbation at home; a stepwise therapeutic approach is recommended.

Bronchodilator Therapy

Home management of COPD exacerbations involves increasing the dose and/or frequency of existing short-acting bronchodilator therapy, preferably with a beta2-agonist (Evidence A). There is not sufficient evidence, however, to indicate a difference in efficacy between the different classes of short-acting bronchodilators, or to indicate additional benefit of combinations of short-acting bronchodilators. However, if not already used, an anticholinergic can be added until the symptoms improve. There is no difference in the clinical response between bronchodilator therapy delivered by metered dose inhaler (MDI) with a spacer and by hand held nebulizer.

Glucocorticosteroids

Systemic glucocorticosteroids are beneficial in the management of exacerbations of COPD. They shorten recovery time, improve lung function (FEV_1) and hypoxemia (PaO_2) (Evidence A), and may reduce the risk of early relapse, treatment failure, and length of hospital stay. They should be considered in addition to bronchodilators if the patient's baseline FEV_1 is <50% predicted. A dose of 30 to 40 mg prednisolone per day for 7 to 10 days is recommended. One large study indicates that nebulized budesonide may be an alternative (although more expensive) to oral glucocorticosteroids in the treatment of non-acidotic exacerbations. Randomized clinical trials in the outpatient office set-up are not available.

Antibiotics

The use of antibiotics in the management of COPD exacerbations is discussed above in the section on assessment of severity and below in the hospital management section.

Hospital Management

The risk of dying from an exacerbation of COPD is closely related to the development of respiratory acidosis, the presence of significant comorbidities, and the need for ventilatory support. Patients lacking these features are not at high risk of dying, but those with severe underlying COPD often require hospitalization in any case. Attempts at managing such patients entirely in the community have met with only limited success, but returning them to their homes with increased social support and a supervised medical care package after initial emergency room assessment has been much more successful. Savings on inpatient expenditures offset the additional costs of maintaining a community-based COPD nursing team. However, detailed cost-benefit analyses of these approaches are awaited.

A range of criteria to consider for hospital assessment/admission for exacerbations of COPD are shown in the Table below.

Indications for Hospital Assessment or Admission for Exacerbations of COPD*
• Marked increase in intensity of symptoms, such as sudden development of resting dyspnea • Severe underlying COPD • Onset of new physical signs (e.g., cyanosis, peripheral edema) • Failure of exacerbation to respond to initial medical management • Significant comorbidities • Frequent exacerbations • Newly occurring arrhythmias • Diagnostic uncertainty • Older age • Insufficient home support *Local resources need to be considered

Some patients need immediate admission to an intensive care unit (ICU) (see Table below). Admission of patient with severe COPD exacerbations to intermediate or special respiratory care units may be appropriate if personnel, skills, and equipment exist to identify and manage acute respiratory failure successfully.

Indications for ICU Admission of Patients with Exacerbations of COPD*
• Severe dyspnea that responds inadequately to initial emergency therapy • Changes in mental status (confusion, lethargy, coma) • Persistent or worsening hypoxemia (PaO_2 <5.3 kPa, 40 mmHg), and/or severe/worsening hypercapnia ($PaCO_2$ >8.0 kPa, 60 mmHg), and/or severe/worsening respiratory acidosis (pH <7.25) despite supplemental oxygen and noninvasive ventilation • Need for invasive mechanical ventilation • Hemodynamic instability—need for vasopressor *Local resources need to be considered

Emergency Department or Hospital

The first actions when a patient reaches the emergency department are to provide supplemental oxygen therapy and to determine whether the exacerbation is life threatening (see Table above). If so, the patient should be admitted to the ICU immediately. Otherwise, the patient may be managed in the emergency department or hospital as detailed below.

Management of Severe by Not Life-Threatening Exacerbations of COPD in the Emergency Department or the Hospital*

• Assess severity of symptoms, blood gases, chest x-ray
• Administer controlled oxygen therapy and repeat arterial blood gas measurement after 30 to 60 minutes
• Bronchodilators:
  • Increase doses and/or frequency
  • Combine $beta_2$-agonists and anticholinergics
  • Use spacers or air-driven nebulizers
  • Consider adding intravenous methylxanthines, if needed
• Add oral or intravenous glucocorticosteroids
• Consider antibiotics (oral or occasionally intravenous) when signs of bacterial infection
• Consider noninvasive mechanical ventilation
• At all times:
  • Monitor fluid balance and nutrition
  • Consider subcutaneous heparin
  • Identify and treat associated conditions (e.g., heart failure, arrhythmias)
  • Closely monitor condition of the patient
 	
*Local resources need to be considered

Controlled Oxygen Therapy

Oxygen therapy is the cornerstone of hospital treatment of COPD exacerbations. Supplemental oxygen should be titrated to improve the patient's hypoxemia. Adequate levels of oxygenation (PaO_2 >8.0 kPa, 60 mm Hg, or SaO_2 >90%) are easy to achieve in uncomplicated exacerbations, but CO_2 retention can occur insidiously with little change in symptoms. Once oxygen is started, arterial blood gases should be checked 30 to 60 minutes later to ensure satisfactory oxygenation without CO_2 retention or acidosis. Venturi masks (high-flow devices) offer more accurate delivery of controlled oxygen than do nasal prongs but are less likely to be tolerated by the patient.

Bronchodilator Therapy

Short-acting inhaled $beta_2$-agonists are usually the preferred bronchodilators for treatment of exacerbations of COPD (Evidence A). If a prompt response to these drugs does not occur, the addition of an anticholinergic is recommended, even though evidence concerning the effectiveness of this combination is controversial. Despite its widespread clinical use, the role of methylxanthines in the treatment of exacerbations of COPD remains controversial. Methylxanthines (theophylline or aminophylline) is currently considered second-line intravenous therapy, used when there is inadequate or insufficient response to short-acting bronchodilators (Evidence B). Possible beneficial effects in terms of lung function and clinical endpoints are modest and inconsistent, whereas adverse effects are significantly increased. There are no clinical studies that have evaluated the use of inhaled long-acting bronchodilators (either $beta_2$-agonists or anticholinergics) with or without inhaled glucocorticosteroids during an acute exacerbation.

Antibiotics

Based on the current available evidence, antibiotics should be given to:

- Patients with exacerbations of COPD with the following three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence (Evidence B)
- Patients with exacerbations of COPD with two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms (Evidence C)
- Patients with a severe exacerbation of COPD that requires mechanical ventilation (invasive or noninvasive) (Evidence B)

Figure 5.4-7 in the original guideline document provides recommended antibiotic treatment for exacerbations of COPD, although it must be emphasized that most of the published studies related to the use of antibiotics were done in chronic bronchitis patients. The route of administration (oral or intravenous [IV]) depends on the ability of the patient to eat and the pharmacokinetics of the antibiotic. The oral route is preferred; if the IV route must be used, switching to the oral route is recommended when clinical stabilization permits. Based on studies of the length of use of antibiotics for chronic bronchitis, antibiotic treatment in patients with COPD exacerbations could be given for 3 to 7 days (Evidence D).

Respiratory Stimulants

Respiratory stimulants are not recommended for acute respiratory failure. Doxapram, a nonspecific but relatively safe respiratory stimulant available in

some countries as an intravenous formulation, should be used only when noninvasive intermittent ventilation is not available or not recommended.

Ventilatory Support

The primary objectives of mechanical ventilatory support in patients with COPD exacerbations are to decrease mortality and morbidity and to relieve symptoms. Ventilatory support includes both noninvasive intermittent ventilation using either negative or positive pressure devices, and invasive (conventional) mechanical ventilation by oro-tracheal tube or tracheostomy.

Noninvasive Mechanical Ventilation

Noninvasive intermittent ventilation (NIV) has been studied in several randomized controlled trials in acute respiratory failure, consistently providing positive results with success rates of 80 to 85%. These studies provide evidence that NIV improves respiratory acidosis (increases pH, and decreases $PaCO_2$) , decreases respiratory rate, severity of breathlessness, and length of hospital stay (Evidence A). More importantly, mortality—or its surrogate, intubation rate—is reduced by this intervention. However, NIV is not appropriate for all patients, as summarized in the Table below.

Indications and Relative Contraindications for NIV
Selection criteria • Moderate to severe dyspnea with use of accessory muscles and paradoxical abdominal motion • Moderate to severe acidosis (pH $\leq$7.35) and/ or hypercapnia ($PaCO_2$ >6.0 kPa, 45 mm Hg) • Respiratory frequency >25 breaths per minute Exclusion criteria (any may be present) • Respiratory arrest • Cardiovascular instability (hypotension, arrhythmias, myocardial infarction) • Change in mental status; uncooperative patient • High aspiration risk • Viscous or copious secretions • Recent facial or gastroesophageal surgery • Craniofacial trauma • Fixed nasopharyngeal abnormalities • Burns • Extreme obesity

Invasive Mechanical Ventilation

During exacerbations of COPD the events occurring within the lungs include bronchoconstriction, airway inflammation, increased mucus secretion, and loss of elastic recoil, all of which prevent the respiratory system from reaching its passive functional residual capacity at the end of expiration, enhancing dynamic

hyperinflation and increasing the work of breathing. The indications for initiating invasive mechanical ventilation during exacerbations of COPD are shown in the Table below, including failure of an initial trial of NIV. As experience is being gained with the generalized clinical use of NIV in COPD, several of the indications for invasive mechanical ventilation are being successfully treated with NIV. Figure 5.4-10 in the original guideline document details some other factors that determine the use of invasive ventilation.

Indications for Invasive Mechanical Ventilation
• Unable to tolerate NIV or NIV failure (or exclusion criteria, see Figure 5.4-8 in the original guideline document) • Severe dyspnea with use of accessory muscles and paradoxical abdominal motion. • Respiratory frequency >35 breaths per minute • Life-threatening hypoxemia • Severe acidosis (pH <7.25) and/or hypercapnia ($PaCO_2$ >8.0 kPa, 60 mm Hg) • Respiratory arrest • Somnolence, impaired mental status • Cardiovascular complications (hypotension, shock) • Other complications (metabolic abnormalities, sepsis, pneumonia, pulmonary embolism, barotrauma, massive pleural effusion)

See the original guideline document for a discussion of other measures that can be used in the hospital.

Hospital Discharge and Follow-Up

Insufficient clinical data exist to establish the optimal duration of hospitalization in individual patients developing an exacerbation of COPD. Consensus and limited data support the discharge criteria listed in the Table below.

Discharge Criteria for Patients with Exacerbations of COPD
• Inhaled $beta_2$-agonist therapy is required no more frequently than every 4 hrs. • Patient, if previously ambulatory, is able to walk across room • Patient is able to eat and sleep without frequent awakening by dyspnea • Patient has been clinically stable for 12 to 24 hrs • Arterial blood gases have been stable for 12 to 24 hrs • Patient (or home caregiver) fully understands correct use of medications • Follow-up and home care arrangements have been completed (e.g., visiting nurse, oxygen delivery, meal provisions) • Patient, family, and physician are confident patient can manage successfully at home

The Table below provides items to include in a follow-up assessment 4 to 6 weeks after discharge from the hospital. Thereafter, follow-up is the same as for stable COPD, including supervising smoking cessation, monitoring the effectiveness of each drug treatment, and monitoring changes in spirometric parameters. Home

visits by a community nurse may permit earlier discharge of patients hospitalized with an exacerbation of COPD, without increasing readmission rates.

Items to Assess at Follow-up Visit 4-6 Weeks After Discharge from Hospital for Exacerbations of COPD
• Ability to cope in usual environment • Measurement of FEV_1 • Reassessment of inhaler technique • Understanding of recommended treatment regimen • Need for long-term oxygen therapy and/or home nebulizer (for patients with Stage IV: Very Severe COPD)

Pharmacotherapy known to reduce the number of exacerbations and hospitalizations and delay the time of first/next hospitalization, such as long-acting inhaled bronchodilators, inhaled glucocorticosteroids, and combination inhalers, should be specifically considered. Early outpatient pulmonary rehabilitation after hospitalization for a COPD exacerbation is safe and results in clinically significant improvements in exercise capacity and health status at 3 months. Social problems should be discussed and principal caregivers identified if the patient has a significant disability.

Definitions:

Description of Levels of Evidence

A. Randomized controlled trials (RCTs). Rich body of data.
   Definition: Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B. RCTs. Limited body of data.
   Definition: Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C. Nonrandomized trials. Observational studies.
   Definition: Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D. Panel consensus. Judgment.
   Definition: This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for the management of an exacerbation of chronic obstructive pulmonary disease (COPD) at home.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is specifically stated for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Chronic obstructive pulmonary disease (COPD) prevention
- The goals of effective COPD management are to:
    - Prevent disease progression
    - Relieve symptoms
    - Improve exercise tolerance
    - Improve health status
    - Prevent and treat complications
    - Prevent and treat exacerbations
    - Reduce mortality

POTENTIAL HARMS

- Arterial Blood Gas Measurement: Adequate pressure must be applied at the arterial puncture site for at least one minute, as failure to do so can lead to painful bruising.
- Beta$_2$-agonists: Stimulation of beta$_2$-receptors can produce resting sinus tachycardia and has the potential to precipitate cardiac rhythm disturbances in very susceptible patients, although this appears to be a remarkably rare event with inhaled therapy. Exaggerated somatic tremor is troublesome in some older patients treated with higher doses of beta$_2$-agonists, whatever the route of administration, and this limits the dose that can be tolerated. Although hypokalemia can occur, especially when treatment is combined with thiazide diuretics, and oxygen consumption can be increased under resting conditions, these metabolic effects show tachyphylaxis unlike the bronchodilator actions. Mild falls in PaO_2 occur after administration of both short- and long-acting beta$_2$-agonists, but the clinical significance of these changes is doubtful. Despite the concerns raised some years ago, further detailed study has found no association between beta$_2$-agonist use and an accelerated loss of lung function or increased mortality in COPD.
- Anticholinergics: Anticholinergic drugs are poorly absorbed, which limits the troublesome systemic effects seen with atropine. Extensive use of this class of inhaled agents in a wide range of doses and clinical settings has shown them to be very safe. The main side effect is dryness of the mouth. Twenty-one days of inhaled tiotropium, 18 micrograms a day as a dry powder, does not retard mucus clearance from the lungs. Although occasional prostatic symptoms have been reported, there are no data to prove a true causal

relationship. A bitter, metallic taste is reported by some patients using ipratropium. An unexpected small increase in cardiovascular events in COPD patients regularly treated with ipratropium bromide has been reported and requires further investigation.

Use of wet nebulizer solutions with a face mask has been reported to precipitate acute glaucoma, probably by a direct effect of the solution on the eye. Mucociliary clearance is unaffected by theses drugs, and respiratory infection rates are not increased.

- Methylxanthines: Toxicity is dose related, a particular problem with the xanthine derivatives because their therapeutic ratio is small and most of the benefit occurs only when near-toxic doses are given. Methylxanthines are nonspecific inhibitors of all phosphodiesterase enzyme subsets, which explains their wide range of toxic effects. Problems include the development of atrial and ventricular arrhythmias (which can prove fatal) and grand mal convulsions (which can occur irrespective of prior epileptic history). More common and less dramatic side effects include headaches, insomnia, nausea, and heartburn, and these may occur within the therapeutic range of serum theophylline. Unlike the other bronchodilator classes, xanthine derivatives may involve a risk of overdose (either intentional or accidental).
- Oral Glucocorticosteroids: A side effect of long-term treatment with systemic glucocorticosteroids is steroid myopathy, which contributes to muscle weakness, decreased functionality, and respiratory failure in subjects with advanced COPD.
- Narcotics (morphine): Some clinical studies suggest that morphine used to control dyspnea may have serious adverse effects and its benefits may be limited to a few sensitive subjects.
- Lung Transplantation: The common complications seen in COPD patients after lung transplantation, apart from operative mortality, are acute rejection and bronchiolitis obliterans, cytomegalovirus (CMV), other opportunistic fungal (Candida, Aspergillus, Cryptococcus, Carinii) or bacterial (Pseudomonas, Staphylococcus species) infections, lymphoproliferative disease, and lymphomas.
- Invasive Mechanical Ventilation: Major hazards include the risk of ventilator-acquired pneumonia (especially when multi-resistant organisms are prevalent), barotrauma, and failure to wean to spontaneous ventilation.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Special consideration should be given before using pharmacotherapy for smoking cessation in selected populations: people with medical contraindications, light smokers (fewer than 10 cigarettes/day), and pregnant and adolescent smokers.
- Nicotine Replacement Therapy: Medical contraindications to nicotine replacement therapy include unstable coronary artery disease, untreated peptic ulcer disease, and recent myocardial infarction or stroke.
- Vasodilators: In patients with stable chronic obstructive pulmonary disease, inhaled nitric oxide can worsen gas exchange because of altered hypoxic regulation of ventilation-perfusion balance and thus is contraindicated.

- Beta-Blockers: Beta-blockers commonly prescribed for heart disease are usually contraindicated in COPD.
- Noninvasive Intermittent Ventilation

Relative Contraindications for Noninvasive Intermittent Ventilation (NIV)

- Respiratory arrest
- Cardiovascular instability (hypotension, arrhythmias, myocardial infarction)
- Change in mental status; uncooperative patient
- High aspiration risk
- Viscous or copious secretions
- Recent facial or gastroesophageal surgery
- Craniofacial trauma
- Fixed nasopharyngeal abnormalities
- Burns
- Extreme obesity

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report is not intended to be a comprehensive textbook on chronic obstructive pulmonary disease (COPD), but rather to summarize the current state of the field.
- A large segment of the world's population lives in areas with inadequate medical facilities and meager financial resources, and fixed international guidelines and rigid scientific protocols will not work in many locations. Thus, the recommendations found in this report must be adapted to fit local practices and the availability of health care resources.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of Chronic Obstructive Pulmonary Disease (COPD) Guidelines

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has developed a network of individuals, the GOLD National Leaders, who are playing an essential role in the dissemination of information about prevention, early diagnosis, and management of COPD in health systems around the world. A major GOLD program activity that has helped to bring together health care teams at the local level is World COPD Day, held annually on the third Wednesday in November (http://www.goldcopd.org/WCDIndex.asp). GOLD National Leaders, often in concert with local physicians, nurses, and health care planners, have hosted many types of activities to raise awareness of COPD. WONCA (the World Organization of Family Doctors) is also an active collaborator in organizing World COPD Day activities. Increased participation of a wide variety of health care professionals in

World COPD Day activities in many countries would help to increase awareness of COPD.

GOLD is a partner organization in a program launched in March 2006 by the World Health Organization, the Global Alliance Against Chronic Respiratory Diseases (GARD). The goal is to raise awareness of the burden of chronic respiratory diseases in all countries of the world, and to disseminate and implement recommendations from international guidelines. Information about the GARD program can be found at http://www.who.int/respiratory/gard/en/.

Although awareness and dissemination of guidelines are important goals, the actual implementation of a comprehensive care system in which to coordinate the management of COPD will be important to pursue. Evidence is increasing that a chronic disease management program for COPD patients that incorporates a variety of interventions, includes pulmonary rehabilitation, and is implemented by primary care reduce hospital admissions and bed days. Key elements are patient participation and information sharing among health care providers.

See Chapter 6 in the original guideline document for more information about translating guideline recommendations to the context of primary care.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary

disease. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization, National Heart, Lung and Blood Institute; 2006. 88 p. [560 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 (revised 2006)

GUIDELINE DEVELOPER(S)

Global Initiative for Chronic Obstructive Lung Disease (GOLD)
National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]
World Health Organization - International Agency

GUIDELINE DEVELOPER COMMENT

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is a collaborative project of the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO).

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GUIDELINE COMMITTEE

Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive Committee
Global Initiative for Chronic Obstructive Lung Disease (GOLD) Science Committee

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*Disclosure forms for GOLD Committees are posted on the GOLD Website, www.goldcopd.org.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Disclosure forms for Global Initiative for Chronic Obstructive Lung Disease (GOLD) Committees are posted on the GOLD Web site.

ENDORSER(S)

American Thoracic Society - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung and Blood Institute (NHLBI). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization, National Heart, Lung and Blood Institute; 2005. 115 p.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute, Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Obstructive Pulmonary Disease Secretariat, Romain Pauwels, M.D., Ph.D., University Hospital, Department of Respiratory Diseases, De Pintelaan 185, B 9000 Ghent BELGIUM; Fax: (32) 9/240 23 41.

AVAILABILITY OF COMPANION DOCUMENTS

The following summary are available:

- Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Executive summary. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization/National Heart, Lung, and Blood Institute; 2006. 28 p. Electronic copies: Available in English and Arabic from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Web site
- Pocket guide to COPD diagnosis, management, and prevention. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization/National Heart, Lung, and Blood Institute; 2006. 28 p. Electronic copies: Available in English and Arabic from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Web site.
- GOLD teaching slide set. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization/National Heart, Lung, and Blood Institute; 2006. Electronic copies: Available from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute, Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Obstructive Pulmonary Disease Secretariat, Romain Pauwels, M.D., Ph.D., University Hospital, Department of Respiratory Diseases, De Pintelaan 185, B 9000 Ghent BELGIUM Fax: (32) 9/240 23 41.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 22, 2001. This summary was updated by ECRI on August 18, 2004, and on October 5, 2005. This summary was updated by ECRI on December 5, 2005 following the U.S. Food and Drug Administration (FDA) advisory on long-acting beta2-adrenergic agonists (LABA). This summary was updated by ECRI on January 27, 2006 following the U.S. Food and Drug Administration (FDA) advisory on Ketek (telithromycin). This summary was updated by ECRI on February 21, 2006 following the U.S. Food and Drug Administration (FDA) advisory on Tequin (gatifloxacin). This summary was updated by ECRI on July 3, 2006 following the updated U.S. Food and Drug Administration (FDA) advisory on Ketek (telithromycin). This NGC summary was

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